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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,303	04/09/2004	Rino Rappuoli	20480.019	3584

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/822,303	RAPPUOLI ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/21/10*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,22,23,25-28,94-98,114,115,117 and 121-134* is/are pending in the application.

4a) Of the above claim(s) *121-126* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *-8, 22, 23, 25-28, 94-98, 114, 115, 117 and 127-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/08;5/21/10;6/21/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the amendment filed on May 21, 2010. Claims 9-21, 24, 29-93, 99-113, 116, and 118-120 have been cancelled. New Claims 133 and 134 have been added. Claims 1-8, 22, 23, 25-28, 94-98, 114, 115, 117 and 121-134 are pending. Claims 121-126 have been withdrawn. Accordingly, Claims 1-8, 22, 23, 25-28, 94-98, 114, 115, 117 and 127-134 are considered in this Office action. The claims are examined to the extent of the elected S polypeptide SEQ ID NO: 6042, and second S1 fragment SEQ ID NO: 7307, and adjuvant MF59 (see Applicants' election filed on May 14, 2008).

Claim Objection

2. (**New objection**) Claim 23 is objected to for being dependent on the withdrawn Claims 121-126. Correction is required.

Claim Rejections - 35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. **(New rejection necessitated by the amendment)** Claims 131 and 132 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 131 and 132 are indefinite. Since SEQ ID NO:6042 appears to be full length S protein, "the polypeptide comprising SEQ ID NO:6042" must include all amino acids of SEQ ID NO:6042, including a transmembrane domain region, a C-terminal cytoplasmic domain. It is not

clear what Claims 131 and 132 are intended by the limitations of "wherein the polypeptide comprising SEQ ID NO:6042 does not include a transmembrane domain region and a C-terminal cytoplasmic domain"; or "wherein the polypeptide comprising SEQ ID NO:6042 fragment does not include up to 70 amino acids of the C-terminus". As a result, one of ordinary skill in the art cannot be reasonably apprised of the metes and bounds of the invention. Appropriate correction is required.

Claim Rejections - 35 USC 112, first paragraph-Scope of Enablement

5. The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior rejection-withdrawn)** The rejection of Claims 22, 23, 25-28, 114, 115 and 117 under 35 USC 112, first paragraph, for failing to comply with the scope of enablement requirement, **is withdrawn** in view of amendment to the claims.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the

United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. **(Prior rejection-maintained-extended and restated necessitated by the amendment)**

The rejection of Claims 2 and 23 under 35 USC 102(e) as being anticipated by Plummer (US20070258999, Provisional application 60/465783, Effective filing date April 28, 2003), as evidenced by Dimitrov (US2006/0240515A1), **is maintained** and **extended** to Claims 1, 4-8, 22, 23, 27, 28, 94 and 133 in view of the amendment.

9. The amended Claims 1, 2, 4-8, 22, 23, 27, 28, 94 and 133 read on an isolated polypeptide, or a fragment thereof, comprising ..., (b) an amino acid sequence having greater than 80% sequence identity to SEQ ID NO: 6042; or (c) at least 10 consecutive amino acids of SEQ ID NO: 6042 (Claims 1 and 133), Applicant has indicated that the support for a fragment "an amino acid sequence have greater than 80% sequence identity to SEQ ID NO: 6042, or at least 10 consecutive amino acids of SEQ ID NO: 6042" is at page 97, line 26 to page 98, line 3 of the instant specification, which is filed April 9, 2004. It is noted that there is no support of the claimed alternatives of SARS spike polypeptide or a fragment thereof, comprising "an amino acid sequence have greater than 80% sequence identity to SEQ ID NO: 6042 (SEQ ID NO: 147), or at least 10 consecutive amino acids of SEQ ID NO: 6042 (SEQ ID NO: 147) " in provisional applications at least prior to 60/473,144, filed on May 22, 2003.

10. Plummer teaches a *S* polypeptide of SARS coronavirus Tor2 strain (S_{Tor2}) shown as SEQ ID NO: 33 (See [0056] and Figure 5), The S_{Tor2} SEQ ID NO: 33 has greater than 80% sequence identity to SEQ ID NO: 6042; or at least 10 consecutive amino acids of SEQ ID NO: 6042. The sequence alignment has been provided to Applicant in the previous Office action. S_{Tor2}

polypeptide is a fusion polypeptide comprising an S1 domain and an S2 domain, of which the S1 domain has a amino acid sequence that is "at least 10 consecutive amino acids of SEQ ID NO: 6042" and is 100% identical the claimed S1 fragment SEQ ID NO: 7307. Plummer teaches that S_{Tor2} glycoprotein SEQ ID NO: 33 belongs to a type I membrane protein with both the *N*-terminus and the majority of the protein (residues 14-1193) on the outside of the cell-surface or virus particle, which may be responsible for binding to a cellular receptor (Para [0084]). This teaching also indicates that S_{Tor2} SEQ ID NO: 33 disclosed by Plummer comprises a surface-exposed fragment of the claimed amino acid sequence SEQ ID NO: 6042, so that meets the limitation of Claim 94. This teaching also inherently teaches that the *S* polypeptide is a trimer (Claim 5). Type I membrane proteins are known to form trimers, as evidenced by Dimitrov. Dimitrov teaches that like viral envelope glycoproteins of class I fusion proteins, the full-length membrane-associated S polypeptide and some soluble peptides thereof are trimeric through the transmembrane domain (Para [0204] and [0207]).

11. Plummer teaches that a SARS virus Spike polypeptide may be suitable for vaccine applications, and the vaccines may be multivalent and include one or more epitopes from a SARS virus polypeptide or fragment thereof (Para [0110]). In view of these teachings, Claims 1, 2, 4-8, 22, 23, 27, 28, 94 and 133 are anticipated by Plummer.

102/103 REJECTION

12. (**Prior rejection-withdrawn**) The rejection of Claims 1, 3-8, 22, 23, 27, 28 and 94 under 35 USC 102(a) as being anticipated by or, in the alternative, under 35 USC 103 as obvious over GenBank AY274119 (submitted on April 13, 2003; The draft of AY274119 was publicly

available on website on April 12, 2003 as evidenced by the website "SARS-associated Coronavirus"(see the attachment to this Office action); as evidenced by Plummer (US20070258999) and Dimitrov (US2006/0240515A1), **is withdrawn** in view of the amendment. A new rejection is set forth below (see Para 15-23). Applicants' argument regarding AY274119 as prior art is considered; see Examiner's response in Para 24-26 below.

Claim Rejections - 35 USC 103

13. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. **(Prior rejection- withdrawn)** The rejection of Claims 25, 26, 95-98, 114, 117 and 127-132 over GenBank AY274119, as applied to Claims 1, 22 and 94 above, further in view of Ksiazek, *et al*. (N Engl J Med. 2003 May 15;348(20):1953-66), Cavanagh *et al* (J Gen Virol. 1986; 67:1435-42); and Song, *et al*. (J Gen Virol. 1998;79 (Pt 4):719-23), **is withdrawn** in view of the amendment. A new rejection necessitated by the amendment is set forth below.

15. **(New rejection necessitated by the amendment)** Claims 1-8, 22, 23, 25-28, 94-98, 114, 115, 117 and 127-134 are rejected over GenBank AY274119 (submitted on April 13, 2003; The draft of AY274119 was publicly available on website on April 12, 2003, as evidenced by the website "SARS-associated Coronavirus", see Attachment (2) provided in the previous Office action), Ksiazek, *et al*. (N Engl J Med. 2003 May 15;348(20):1953-66. Epub 2003 Apr 10),

(Tomley F. *et al*. (J. Gen. Virology, 68:2291-2298;1987); Cavanagh *et al* (J Gen Virol. 1986; 67:1435-42; cited in previous Office action); and Delmas B. *et al*. (J. Virology; 64(11):5367-5375;1990).

16. GenBank AY274119 discloses the genome of SARS coronavirus Tor2 strain (S_{Tor2}), which encodes a S polypeptide of SARS coronavirus Tor2 strain (S_{Tor2}) 100% identical to the claimed polypeptide SEQ ID NO: 6042. The sequence alignment was provided to Applicant with the previous Office action, see Attachment (3).

17. AY274119 does not explicitly teach the following embodiments: (1) S polypeptide fusion protein, trimer; or fragments that do not include the last 50 or 70 amino acids of the *C*-terminus of SEQ ID NO: 6042; or an *N*-signal peptide and/or a *C*-terminal transmembrane domain (e.g. Claims 4-6 and 95-98); (2) A method of vaccinating a subject using the *S* peptide (Claims 117 and 134); and (3) use of MF59 as an *S* protein subunit vaccine adjuvant (Claims 26, 114 and 115)

18. Ksiazek teaches a novel SARS-cornonavirus, which is identified as the etiologic agent for the outbreak of SARS in humans, see e.g. Abstract. SARS virus is closely related to animal coronaviruses, such as avian IBV (infectious bronchitis virus), see e.g. Fig.3, p.1959. Ksiazek indicates that there is a need to develop strategies, especially strategies for developing vaccines, to control newly emerged SARS virus, see e.g. Para 1, right col. p. 1964.

19. Tomley teaches a method of stimulating an immune response in mice using a fusion protein of S protein (S1 plus S2); see e.g. Abstract. Tomley teaches that the spike protein of IBV is a target for virus-neutralizing antibodies, therefore, is an excellent candidate for use in IBV vaccine, see e.g. last para, p. 2295.

20. Cavanagh teaches a polypeptide of S1 subunit of *S* protein from IBV (a coronavirus), which does not include the amino acids corresponding to "the last 50 or 70 amino acids of the *C*-terminus of SEQ ID NO: 6042", and does not include "a *C*-terminal transmembrane domain", See e.g. *Introduction*, Para 1, p. 1435. Cavanagh also teaches a method for preventing coronavirus infection using the S1 polypeptide and adjuvant, see Para 1, p.1436. Cavanagh showed that the S1 subunit is the major inducer of virus neutralizing antibodies (Whole document, particularly p. 1440-1442). Vaccination of chickens with the S1 subunit was able to induce virus-neutralizing antibodies, but a virus that lacked the S1 subunit was unable to induce neutralizing antibody (Title, pp. 1439-1442).

21. Delmas teaches that coronavirus S protein from trimers presents major antigenic sites for neutralizing antibodies; see e.g. Abstract, and Para 2 and 3, left col. p. 5374.

22. Gasparini teaches MF59 adjuvant, see e.g. Abstract. Gasparini also teaches that through statistical analysis, it was shown that more subjects developed enhanced immunogenicity who received subunit influenza vaccine with adjuvant MF59 than those who received conventional subunit influenza antigens without MF59 (p. 137).

23. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the claimed S protein of SEQ ID NO:6042 and S1 fragment of SEQ ID NO:7307 as a vaccine candidate. In the case of *KSR International Co. v. Teleflex Inc.* (82 U.S.P.Q. 2d1385, 2007), the Supreme Court provided a number of bases on which a claimed invention may be found obvious. In particular, "When there is a design need or market pressure to solve a problem and there are a finite number of identified predictable potential solutions, a person of ordinary skill has good reason to pursue the known potential options within his or her

technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense". In the present case, first, the prior art indicates that there is a known need/desire in the art to develop make a vaccine to control the newly emerged human SARS coronavirus, as shown by Ksiazek. Secondly, the prior art has provided a finite number of identified predictable potential solutions for making the S fusion protein (e.g. SEQ ID NO: 6042) or S1 fragments (e.g. SEQ ID NO: 7307) as a vaccine candidate. Specifically, Ksiazek has taught one of ordinary skill in the art that newly emerged SARS-cornonavirus is closely related to animal coronaviruses, such as avian IBV (infectious bronchitis virus), see e.g. Fig.3, p.1959. AY274119 has provided the full sequence of the SARS genome, including the sequence of the S protein. It is within the ability of one of ordinary skill in the art to identify the sequences of SARS proteins from AY274119, including S proteins of SEQ ID NOs: 6042 and 7307 based on the knowledge of other coronaviruses, as shown by Ksiazek. Both Tomley and Cavanagh have provided teachings indicating that S protein and *S*1 fragments are critical and sufficient to induce virus-neutralizing antibodies and protective immunity against animal coronaviruses. Finally, the prior art shows that those of ordinary skill in the art were able to pursue the known potential options with a reasonable expectation of success in making/using the specific S1 fragments. For instance, one of ordinary skill in the art was capable of acquiring knowledge of newly emerged SARS virus from the analogous art of known animal coronaviruses as shown by Ksiazek. One of ordinary skill in the art was also capable of making the spike protein and S1 fragment using routine lab practice, and testing the S1 polypeptide in animals, as shown by both Tomley and Cavanagh. Thus, one skilled in the art would have a reasonable expectation of success in making and using the claimed S protein and S1 fragments of SARS for

inducing immune response, given that the sequence of the S gene was available at the time the application was filed, and also given the success of the prior art that S protein and S1 fragment are sufficient to induce immune response as shown by both Tomley and Cavanagh. One skilled in the art would also a reasonable expectation of success in using the adjuvant MF59, given that MF59 can enhance the immunogenicity of subunit peptide antigens, as taught by Gasparini. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In response to Applicant's argument:

24. Applicant argues that Genbank AY274119 is not prior art to Applicants' priority date of April 13, 2003, because SEQ ID NO: 147, which is identical to the Spike protein of SEQ ID NO: 6042, is disclosed on page 39 in Serial No. 60/462,748, filed on April 13, 2003, which means that SEQ ID NO: 6042 has a priority date of April 13, 2003. Second, Exhibit 2 establishes that AY274119 was not publicly available until April 14, 2003, at 10:49 AM, after Applicant's April 13, 2003, priority date. Exhibit 3 establishes that the AY274119 sequence disclosed on April 14, 2003, contains only the SARS genome sequence and lacks any description of particular SARS proteins. None of Ksiazek, Cavanagh, Song, or Gasparini teach a SARS Spike protein. Therefore, the Patent Office has not made *a prima facie* case of obviousness.

25. Applicant's argument is considered, but found not persuasive for the following reasons: First, the previous Office action has provided a copy of "website "SARS-associated Coronavirus", which shows that the draft genome sequence of SARS Tor2, AY274119, was publicly available on April 12, 2003; see Attachment (2). It is also noted that Applicant's

provisional application 60/462,748, filed on April 13, 2003, states: "The Genome Science Center in British Colombia, Canada has published on their website (http://www.bcgsc.ca/bioinfo/SARS/) a draft genome assembly of 29,736 base pairs of a virus believed to be a SARS virus, referred to as the Tor2 isolate. This draft genome assembly is attached as FIGURE 301" (Para 1, p. 2). Thus, Applicant confirms that the draft of AY274119, which contains the sequence of 29,736 base pairs of Tor2,
was publicly available prior to the time when 60/462,748 was filed. Furthermore, as evidenced, Leung indicates: "The Canadian British Columbia Cancer Agency and the U.S. Centers for Disease Control groups posted their SARS coronavirus genome sequences on the Internet on 12 and 14 April, respectively"; see Para 2, right co. p. 309 (*Science* 31 July 2003:Vol. 301. no. 5631, pp. 309-310). Thus, the draft genome sequence of SARS Tor2, AY274119, was publicly available on April 12, 2003.

26. Secondly, the claims as amended are not limited to SEQ ID NO: 6042. The amended Claims 1-8, 22, 23, 27, 28, 94 and 133 read on an isolated polypeptide, or a fragment thereof, comprising (a) a SARS coronavirus Spike (S) polypeptide SEQ ID NO: 6042, (b) an amino acid sequence having greater than 80% sequence identity to SEQ ID NO: 6042; or (c) at least 10 consecutive amino acids of SEQ ID NO: 6042 (Claims 1 and 133), wherein the fragment is the *S*1 domain of SEQ ID NO: 7307. Applicant has indicate that the support for a fragment "an amino acid sequence have greater than 80% sequence identity to SEQ ID NO: 6042, or at least 10 consecutive amino acids of SEQ ID NO: 6042" is at page 97, line 26 to page 98, line 3 of the instant specification, which was filed April 9, 2004. Thus, Genbank AY274119 is proper prior art for Claims 1-8, 22, 23, 27, 28, 94 and 133.

27. (**Restated rejection necessitated by the amendment**) Claims 95-98 are rejected under 35 USC 103(a) as being unpatentable over Plummer (US20070258999), as applied to Claim 94 above, in view of Cavanagh D. *et al* (J Gen Virol. 1986 Jul;67:1435-42).

28. Claims 95-98 are directed to the polypeptide of Claim 94, wherein said fragment does not include the last 50 amino acids of the *C*-terminus of SEQ ID NO: 6042, wherein said fragment does not include a transdomain region of SEQ ID NO: 6042, wherein said fragment does not include a *C*-terminus cytoplasmic domain of SEQ ID NO: 6042, and wherein said fragment does not include a *N*-terminus signal sequence.

29. The relevance of Plummer is set forth *supra*. Moreover, Plummer teaches that SEQ ID NO: 33 contains a signal peptide (MFIFLLFLTLTSG; SEQ ID NO: 76) from amino acids 1-13 at its *N*-terminus, and a transmembrane domain WYVWLGFIAGLIAIVMVTILLCC from amino acids 1194 to 1216, which is about 60 amino acids of the *C*-terminal end of S_{Tor2} SEQ ID NO: 33. Plummer teaches that residues 14-1193 of S_{Tor2} SEQ ID NO: 33 are on the outside of the cell-surface or virus particle, which may be responsible for binding to a cellular receptor (Para [0084]).

30. Plummer does not explicitly teach making S_{Tor2} peptide fragments lacking an *N*-signal peptide and/or a *C*-terminal transmembrane domain.

31. Cavanagh teaches that the *S*1 subunit of IBV spike protein, which lacks a *C*-terminal transmembrane domain (*S*2 subunit), is the major inducer of virus-neutralizing antibodies (Whole document, particularly pp. 1440-1442). Cavanagh teaches that vaccination of chickens with the *S*1 subunit alone was able to induce virus-neutralizing antibodies, but virus that lacked

the *S*1 subunit was unable to induce neutralizing antibody (Title, pp. 1439-1442).

32. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make S_{Tor2} peptide fragments lacking an *N*-signal peptide and/or a *C*-terminal transmembrane domain as a vaccine component. One skilled in the art would have been motivated to generate the claimed S_{Tor2} peptide fragments, and have a reasonable expectation of success that such fragments are immunogenic and can induce neutralizing antibodies, given the knowledge that the surface-exposed fragment of SEQ ID NO: 6042, but not an *N*-signal peptide and the *C*-terminal 50 amino acids of SEQ ID NO: 6042 containing the transmembrane domain, is responsible for receptor binding and induction of neutralizing antibodies, as taught by Plummer and Cavanagh. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

33. (**Restated rejection necessitated by the amendment**) Claims 25, 26, 114, 115 and 117 are rejected under 35 USC 103(a) as being unpatentable over Plummer (US 20070258999), as applied to Claim 22 above, in view of Gasparini *et al*. (European Journal of Epideminology 17:135-140, 2001).

34. Claims 25, 26, 114 and 115 are directed to the immunogenic composition of Claim 22 further comprising an adjuvant, wherein the adjuvant is MF59. Claims 117 and 134 are directed to a method of stimulating an immune response in a subject comprising administering to the subject immunogenic compositions of Claims 22 and 133.

35. The relevance of Plummer is set forth *supra*.

36. Plummer does not teach use of either MF59 as a vaccine adjuvant, or a method of vaccinating a subject using the S peptide of Claim 22.

37. Gasparini teaches a method of vaccinating a subject using the MF59-adjuvanted influenza subunit vaccine comprising surface antigens of influenza virus (entire document, particularly Abstract). Gasparini teaches that a subunit influenza vaccine with adjuvant MF59 is more immunogenic. Statistical analysis showed that more subjects developed enhanced immunogenicity to SARS CoV who received subunit influenza vaccine with adjuvant MF59 than those who received conventional subunit influenza antigens without MF59 (p. 137).

38. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use an adjuvant like MF59 with alleged SARS *S* peptide vaccine for the purpose of enhancing the immunogenicity of the alleged subunit vaccine. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success, given the knowledge that vaccine adjuvant, like MF59, can enhance the immunogenicity of subunit peptide antigens, as taught by Gasparini. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Remarks

39. No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648